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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/667,856	09/22/2003	Rachel Courtney	IN01630	1369

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SCHERING-PLOUGH CORPORATION
PATENT DEPARTMENT (K-6-1, 1990)
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EXAMINER	
KANTAMNENI, SHOBHA	
ART UNIT	PAPER NUMBER
1617	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/22/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

TL

Office Action Summary	Application No.	Applicant(s)	
	10/667,856	COURTNEY ET AL.	
	Examiner	Art Unit	
	Shobha Kantamneni	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *NONE* is/are allowed.

6)☒ Claim(s) *1-31* is/are rejected.

7)☒ Claim(s) *15, 19, 24, 28, 30-31* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *05/07/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Priority

This application filed on 09/22/2003, claims benefit of 60/412,985 filed on 09/23/2002.

Claims 1-31 are pending, and examined herein.

Claim Objections

Claims 15, 19, 24, 28, 30-31 are objected to because of the following informalities:

The word patient on line 4 claim 28 is spelt wrong.

The word "of" is missing after the word "method" in line 1 of claims 15, 19, 24, 30-31. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating fungal infections in humans comprising administering an effective amount of posaconazole **does not reasonably provide enablement for a method of preventing fungal infections**. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention **commensurate in scope** with these claims.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1) The Nature of the Invention:

The rejected claims are drawn to a method of treating or **preventing** fungal infections in humans comprising administering an effective amount of posaconazole.

(2) Breadth of the Claims:

The instant claims embrace a method of treating or **preventing** a variety of fungal infections in humans including but not limited to invasive fungal infection, refractory fungal infection etc..

(3) Guidance of the Specification / Working Examples:

In the instant case, no working examples are presented in the specification as filed showing how to prevent fungal infection in human by orally administering an effective amount of posaconazole totally, absolutely, or permanently, not even occurring at the first time.

(4) State/predictability of the Art:

The relative skill of those in the art is high.

It is well-known in the state of the art that fungal infections are caused by various fungi. Several drugs effective against fungal infections are available, but the structure and chemical makeup of fungi make them difficult to kill. It is known that some of the fungal infections are resistant to standard fungal therapies including but not limited to those therapies employing fluconazole, itraconazole or amphothericin B. See, instant specification page 7, lines 12-15. Thus the skilled artisan would view that the ability to prevent fungal infections by administering posaconazole in a human or animal totally, absolutely or permanently, not even occurring at the first time is highly unpredictable.

(5) The Quantity of Experimentation Necessary:

Applicant fails to provide information sufficient to practice the claimed invention, absent undue experimentation.

Genetech, 108 F.3d at 1366 states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors, e.g., the amount of direction or guidance provided, absence of working examples, and the predictability of the art discussed above, to practice the claimed invention herein, a person of skill in the art would have to test posaconazole against various fungi in the instant claims to be administered to a

host employed in the claimed methods of the particular treatments herein, with no assurance of success.

Accordingly the claims are evaluated as a method of treating fungal infections in human and not a method of **preventing** fungal infections.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-7, 9-13, 15-17, 19-21, 23-26, 28-29, 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Winston et al. (Blood, November 16, 2000, Vol.96, No.11 part 2, pp. 341b, PTO-1449).

Winston et al. discloses a method of treating invasive fungal infections in humans of 12 years and older comprising administering an effective amount of posaconazole. Administration of 200 mg posaconazole po qid for 1 week resulted in clinical improvement i.e 200 mg of posaconazole 4 times a day orally, and after 6 months of administration of 400 mg po bid to a 45-year old man neutropenic patient, and immuno-compromised patient resulted in almost complete radiographic resolution. See the entire abstract.

Regarding the limitations wherein "administering an effective amount of posaconazole in divided doses two to four times a day to produce an arithmetic mean

steady state average maximum plasma concentration of posaconazole of at least about 300 ng/mL to at least about 520 ng/mL, wherein the arithmetic mean steady state maximum plasma concentration (Cmax) of posaconazole of at least about 300 ng/mL to about 320 ng/mL is produced at a mean time (Tmax) after the initial dose in the range of about 12 hours to about 21 hours, wherein a plot of the plasma concentration of posaconazole over time yields an arithmetic mean AUC (0-24hr) for posaconazole in the range of about 7,700 ng.hr/mL to about 12,400 ng.hr/mL," etc. in the instant claims are functional limitations, and are inherently present in Winston et al. method steps because Winston discloses the administration of the same effective amounts of posaconazole i.e 200 mg four times a day, 400 mg two times a day to the same or overlapping patient population.

Regarding the limitation "arithmetic mean steady state average maximum plasma concentration of posaconazole that exceeds the majority of the Minimum Inhibitory Concentrations needed to kill 90 % of the clinically relevant pathogenic fungi" in claim 23, Winston et al. disclose the oral administration of posaconazole in the same effective amounts as instantly claimed and meets the limitation.

Winston et al. anticipate instant claims 1-7, 9-13, 15-17, 19-21, 23-26, 28-29, 31.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 8, 14, 18, 22, 27, 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Winston et al. as applied to claims 1-7, 9-13, 15-17, 19-21, 23-26, 28-29, 31 above.

Winston et al. does not specifically teach the particular treatment regimen administration of about 800 mg of posaconazole a day in three divided doses as in claim 30, and wherein posaconazole is administered to a patient before food in take, i.e fasted patient as in claims 8, 14, 18, 22, and 27.

It would have been obvious to a person of ordinary skill in the art at the time of invention to administer 800 mg of posaconazole a day in three divided doses.

It would have been obvious to a person of ordinary skill in the art at the time of invention to administer posaconazole to a patient before food intake.

One having ordinary skill in the art at the time the invention was made would have been motivated to the particular treatment because the optimization of result effect parameters such as dosage range, dosing regimen is obvious and is considered well in the competence level of an ordinary skilled artisan in pharmaceutical science, involving merely routine skill in the art.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4, 9-11, 15, 19, 23-24, 28-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Saksena et al. (US 5,661,151, PTO-1449).

Saksena et al. discloses a method of treating fungal infections in humans of 12 years and older which comprises orally administering an effective amount of posaconazole. See abstract; column 3, formula III; column 9-column 11. It is disclosed that the oral dosage for humans for antifungal use ranges from about 1 mg per kilogram of body weight to about 30 mg per kilogram of body weight per day, in single or divided doses. It is also taught that the exact amount, frequency and period of administration will vary, depending upon the sex, age and medical condition of the patient as well as the severity of the infection as determined by the attending clinician. See column 58, line 64-column 59, line 14; column 78, claims 11-13.

Saksena et al. do not explicitly teach the particular treatment regimen such as administration of posaconazole in divided doses two to four times a day, about 200 mg 4 times a day, about 400 mg two times a day, a total dose of about 800 mg of posaconazole a day in three divided doses.

It would have been obvious to a person of ordinary skill in the art at the time of invention to employ the particular treatment regimen.

One of ordinary skill in the art at the time of invention would have been motivated to employ the particular treatment regimen because Saksena et al. broadly teaches that the dosage, frequency and period of administration will vary, depending upon the sex, age and medical condition of the patient as well as the severity of the infection as determined by the attending clinician. Further, the optimization of result effect parameters such as dosage range, dosing regimen is obvious and is considered well in the competence level of an ordinary skilled artisan in pharmaceutical science, involving merely routine skill in the art.

Regarding the limitations wherein "administering an effective amount of posaconazole in divided doses two to four times a day to produce an arithmetic mean steady state average maximum plasma concentration of posaconazole of at least about 300 ng/mL to at least about 520 ng/mL, wherein the arithmetic mean steady state maximum plasma concentration (Cmax) of posaconazole of at least about 300 ng/mL to about 320 ng/mL is produced at a mean time (Tmax) after the initial dose in the range of about 12 hours to about 21 hours, wherein a plot of the plasma concentration of posaconazole over time yields an arithmetic mean AUC (0-24hr) for posaconazole in the range of about 7,700 ng.hr/mL to about 12,400 ng.hr/mL," etc. in the instant claims are functional limitations, and by optimizing the result effect parameters such as those discussed above will meet these limitations.

Conclusion

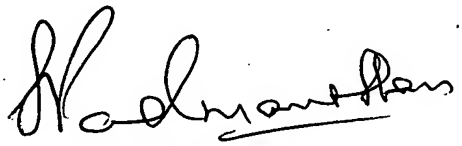
No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shobha Kantamneni whose telephone number is 571-272-2930. The examiner can normally be reached on Monday-Tuesday, Thursday-Friday, 8am-4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, Ph.D can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Shobha Kantamneni, Ph.D
Patent Examiner
Art Unit : 1617



SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER